Role of Pre-Operative Blood Transfusion and Subcutaneous Fat Thickness as Risk Factors for Surgical Site Infection after Posterior Thoracic Spine Stabilization

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Abstract: BACKGROUND Surgical site infections (SSIs) increase morbidity and mortality rates and generate additional cost for the healthcare system. Pre-operative blood transfusion and the subcutaneous fat thickness (SFT) have been described as risk factors for SSI in other surgical areas. The purpose of this study was to assess the impact of pre-operative blood transfusion and the SFT on the occurrence of SSI in posterior thoracic spine surgery. METHODS In total, 244 patients (median age 55 y; 97 female) who underwent posterior thoracic spine fusions from 2008 to 2012 were reviewed retrospectively. Patient-specific characteristics, pre-operative hemoglobin concentration/hematocrit values, the amount of blood transfused, and the occurrence of a post-operative SSI were documented. The SFT was measured on pre-operative computed tomography scans. RESULTS Surgical site infection was observed in 26 patients (11%). The SFT was 13 mm in patients without SSI and 14 mm in those with infection (p=0.195). The odds ratio for patients with pre-operative blood transfusion to present with SSI was 3.1 (confidence interval [CI] 1.4-7.2) and 2.7 (CI 1.1-6.4) when adjusted for age. There was no difference between the groups with regard to pre-operative hemoglobin concentration (p=0.519) or hematocrit (p=0.908). The SFT did not differ in the two groups. CONCLUSIONS Allogeneic red blood cell transfusion within 48 h prior to surgery was an independent risk factor for SSI after posterior fusion for the fixation of thoracic spine instabilities. Pre-operative blood transfusion tripled the risk, whereas SFT had no influence on the occurrence of SSI.

DOI: https://doi.org/10.1089/sur.2014.081

SURGICAL INFECTIONS
Volume 16, Number 3, 2015

DOI: 10.1089/sur.2014.081

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Abstract

Background: Surgical site infections (SSIs) increase morbidity and mortality rates and generate additional cost for the healthcare system. Pre-operative blood transfusion and the subcutaneous fat thickness (SFT) have been described as risk factors for SSI in other surgical areas. The purpose of this study was to assess the impact of pre-operative blood transfusion and the SFT on the occurrence of SSI in posterior thoracic spine surgery.
Methods: In total, 244 patients (median age 55 y; 97 female) who underwent posterior thoracic spine fusions from 2008 to 2012 were reviewed retrospectively. Patient-specific characteristics, pre-operative hemoglobin concentration/hematocrit values, the amount of blood transfused, and the occurrence of a post-operative SSI were documented. The SFT was measured on pre-operative computed tomography scans.
Results: Surgical site infection was observed in 26 patients (11%). The SFT was 13 mm in patients without SSI and 14 mm in those with infection ($p = 0.195$). The odds ratio for patients with pre-operative blood transfusion to present with SSI was 3.1 (confidence interval [CI] 1.4–7.2) and 2.7 (CI 1.1–6.4) when adjusted for age. There was no difference between the groups with regard to pre-operative hemoglobin concentration ($p = 0.519$) or hematocrit ($p = 0.908$). The SFT did not differ in the two groups.
Conclusions: Allogeneic red blood cell transfusion within 48 h prior to surgery was an independent risk factor for SSI after posterior fusion for the fixation of thoracic spine instabilities. Pre-operative blood transfusion tripled the risk, whereas SFT had no influence on the occurrence of SSI.

Surgical site infections (SSIs) account for 38% of all hospital-acquired infections after surgery [1] and have been linked to higher treatment costs and prolonged hospital stays [2–4]. The rate of SSI after spinal surgery is reported to range from 1% to 17% [4–8]. Factors such as diabetes mellitus, metastatic malignant disease, obesity, smoking, and long duration of surgery appear to influence the occurrence of incisional infections after spinal surgery [4,9].

Recently, two additional factors have been discussed. Mehta et al. reported an association between subcutaneous fat thickness (SFT) and SSIs after posterior cervical spine fusion surgery, this being an independent risk factor [10]. In the cervical area, there usually is a distinct layer of well-perfused musculature between the skin and spine. However, in the thoracic spine, the combination of kyphosis and less soft tissue coverage leads to a closer relation of bone (and implant) and skin. The first hypothesis of this study was that there is a higher risk of infection after posterior thoracic spine fusion in patients with a low SFT.

A purported association between pre-operative blood transfusion and a higher rate of SSIs has been controversial [11–15]. Some authors presume immuno-suppressive effects as a reaction to allogenic transfusions to be responsible for a higher rate of malignant disease recurrence and nosocomial infections [15–17]. The second hypothesis of this study was that there is a higher risk of SSI if blood has been transfused within 48 h prior to the intervention. Thus, the aims of the study were to assess SFT and pre-operative blood transfusion as potential independent risk factors for SSI after posterior fusion for the fixation of thoracic spine instabilities.

Patients and Methods

A single-center retrospective cohort study was conducted at a university-level 1 trauma center through review of charts. This study was approved by the local institutional ethics

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committee (Kantonale Ethikkommission Zürich; Ref. No. 2013-0293).

Patients

Two hundred eighty-eight consecutive patients aged ≥ 18 y who were treated for thoracic spine instabilities by posterior thoracic spine fusion between January 2008 and December 2012 were included in this study. Thoracic spine instabilities comprised traumatic sequelae and pathologic fractures secondary to spinal metastases. Posterior thoracic spine fusion was defined as an intervention that included or bridged at least one injured thoracic segment. The standard intervention was performed with the patient prone using a posterolateral approach to the thoracic spine with reposition and fixation of the fracture by an internal fixateur (USS II, Synthes, Oberdorf, Switzerland, or Legacy, Medtronic, Fridley, MN). If the autologous bone harvested from the thoracic site was believed not to be enough to achieve posterior fusion, additional allograft (demineralized bone matrix) was applied. All patients received intravenous single-dose antibiotic prophylaxis (cefazolin) 30 min prior to surgery. If necessary, allogeneic transfusion management and treatment of a potential trauma-associated coagulopathy during the hospital stay followed a fixed algorithm [18].

The surgical algorithm emphasizes the use of antifibrinolytics, point-of-care testing, and coagulation algorithms with substitution of factor concentrates to allow a reduction of allogeneic transfusion volume. According to this algorithm, blood transfusion was given if the hemoglobin concentration was < 70 g/L in healthy patients, < 80 g/L in patients with increased risk under impaired oxygenation (e.g., traumatic brain injury, coronary artery disease, age > 80 y), and < 90 g/L in patients with severe coronary artery disease or severe heart failure.

Frequent routine follow-up included clinical assessment and blood tests for inflammatory parameters in patients at risk. In the case of pre-operative blood transfusion, hemoglobin and hematocrit measurements were made after transfusion and before surgery. Patients with pre-operative infection or revision surgery (n = 15); patients with missing records on history, medication, transfusions during the hospital stay, and duration of surgery (n = 0); and patients with an infection-free post-operative follow-up of less < 30 d (n = 14) were excluded. In addition, we excluded patients with missing or insufficient pre-operative computed tomography (CT) imaging, ''insufficient'' meaning that we were unable to measure SFT (n = 15). Finally, 244 patients (median age 55 y, range 18–91 y; 97 female) were included.

Data Acquisition

Patient-specific and demographic characteristics with a special focus on the presence of diabetes mellitus, pre-operative local radiation therapy, an immunodeficiency (human immunodeficiency virus, tuberculosis) or immunosuppressive medication, pre-operative hemoglobin, amount of pre-operative allogeneic red blood cell transfusions, and the duration of surgery were documented.

Subcutaneous fat thickness was defined as the the distance from the skin surface to the muscular fascia in the median plane on axial and sagittal views of pre-operative CT scans as described previously for the cervical spine [10]. Measurements were performed by one of the authors (LB). Each measurement was repeated three times, and means were calculated. Post-operative SSI was said to be present in case of incision drainage or the presence of an abscess with at least one positive culture, as well as any delay in wound healing that was treated by antibiotics or surgical revision.

Statistical Analysis

Statistical analysis was performed by an institutional statistician. All data were recorded in an Excel database (Microsoft Corp., Washington, DC) and exported to SPSS 21.0 (IBM, Inc., Armonk, NY) for analysis. Unless otherwise denoted, data were summarized as the mean with the standard deviation (SD).

The primary outcome was the occurrence of an SSI within six wks after surgery. A regression analysis was performed to assess ''subcutaneous fat thickness'' and ''pre-operative blood transfusion'' as potential independent risk factors for SSI. To detect potential confounders such as age, diabetes mellitus, pre-operative local radiation therapy, immunodeficiency, immunosuppressive medication, number of instrumented spinal segments, and the duration of surgery, crosstabs were associated. Where applicable, nominal variables crosstabs were associated using χ^2 or Fisher exact tests. Because the variables exhibited somewhat non-normal distributions, a nonparametric analysis (Mann-Whitney U test) was used to compare continuous data. In the case of a significant association, this variable was further analyzed by regression. To determine the prognostic value of SFT and pre-operative blood transfusion, an odds ratio with a confidence interval (CI) of 95% was calculated, and a receiver-operating characteristic curve (ROC) analysis was generated with calculation of the area under the curve (c statistic). To test for potential autocorrelation, cases were sorted by date of surgery and tested for randomness using a Wald-Wolfowitz test. The level of significance was defined as $p < 0.05$.

Results

Surgical site infection was observed in 26 patients (11%). The mean interval between surgery and diagnosis of an infection was 19 d (median 18 d; range 7–42 d). The pathogenic micro-organism cultures were coagulase-negative staphylococci (n = 10), *Staphylococcus aureus* (n = 8), *Acinetobacter baumannii* (n = 1), and *Enterococcus faecalis* (n = 1). In six cases, no micro-organism was recovered or no samples were taken for culture.

The presence of diabetes mellitus (6%), pre-operative local radiation therapy (5%), immunodeficiency (1%), immunosuppressive medication (4%), the number of instrumented spinal segments (5 ± 2), and gender were equally distributed in the group of patients with and without SSI (Table 1). In both groups, the initial reason for thoracic spine instability was traumatic in 80% and metastatic disease in 20% ($p = 0.617$; Table 1). The duration of surgery was not longer in patients who presented with an infection at a later date ($p = 0.054$). By contrast, there was a significant difference in age between the two groups, with patients having infection being older (Table 1).

The SFT was 13 ± 7 mm in patients without SSI and 14 ± 6 mm in those with an infection. This difference was not

Table 1. Patients' Baseline Characteristics

	Infection			
	Yes	*No*	p	*Total*
No.	26	218		244
Age (y [SD])	61 (15)	53 (18)	0.021[b]	54 (17)
Gender (F:M)	11:15	86:132	0.778[a]	97:147
Duration of surgery (min [SD])	190 (112)	154 (84)	.054[b]	157 (88)
No. of involved spinal segments (SD)	5 (2)	5 (2)	.531[b]	5 (2)
Co-morbidities (%)				
Diabetes mellitus	2 (8)	13 (6)	.666[a]	15 (6)
Pre-operative radiation therapy	0	11 (5)	.24 [a]	11 (5)
Malignant disease	5 (19)	42 (19)	.617[a]	47 (19)
Immunodeficiency	1 (4)	1 (< 1)	.997[a]	2 (1)
Immunosuppressive medication	0	9 (4)	.391[a]	9 (4)

[a]Pearson χ^2/Fisher exact test.
[b]Mann-Whitney U test.
SD = standard deviation.

significant (p = 0.195; Mann-Whitney U test). Thus, further regression analysis for this factor was abandoned.

Twelve of 26 patients with an SSI (46%) had received pre-operative blood transfusion, whereas this was the case in only 47 of 171 patients (22%) without infection (p = 0.006; Pearson χ^2). Blood transfusion within 48 h prior to surgery was confirmed as an independent risk factor for SSI after posterior fusion for stabilization of thoracic spine trauma by regression analysis (coefficient $B = 1.137$; p = 0.009; c statistic 0.62, 95% CI 0.50–0.74; Wald-Wolfowitz p = 0.31). The odds ratio (OR) for patients with pre-operative blood transfusion to present with an SSI was 3.1 (95% CI 1.4–7.2; p = 0.008). As age older than 60 y also was associated with incision infection (OR 1.0; 95% CI 1.0–1.1; p = 0.100), we performed a regression analysis that was adjusted for age. In this age-adjusted analysis, the OR for patients with pre-operative blood transfusion to sustain an SSI remained 2.7 (95% CI 1.1–6.4; p = 0.024; Hosmer-Lemeshow p = 0.270; c statistic 0.69; 95% CI 0.59–0.79; Wald-Wolfowitz p = 0.16; Fig. 1).

Patients with a post-operative SSI also had been given a larger number of pre-operative blood units than patients without infection (1.2 ± 1.7 units vs. 0.7 ± 1.9 units; p = 0.009). By contrast, there was no difference between the groups with regard to pre-operative hemoglobin concentration (11.9 ± 1.7 g/L vs. 12.1 ± 2.3 g/L; p = 0.519) or hematocrit (35.6% ± 4.8% vs. 35.2% ± 7.1%; p = 0.908).

Discussion

The purpose of this study was to assess SFT and pre-operative blood transfusion as independent risk factors for SSI after posterior fusion for the fixation of thoracic spine instabilities.

In contrast to a recent study on cervical spine fusion surgery [10], SFT did not seem to play an important role as a risk factor for infection in the population of the present study. The main reasons for this might be differences in anatomy between the cervical and thoracic spine with a different curvature and different muscle–fat ratios. It is possible that SFT is of importance in areas where there is more soft tissue than rostral to the thoracic spine [10,19,20].

On the other hand, pre-operative allogeneic blood transfusion proved to be an independent risk factor for SSI, tripling the risk of incisional SSI. This is in line with a recent large retrospective matched case-control study that reported an association between SSI after lumbar spine surgery and the volume of peri-operative allogeneic red blood cell transfusion [14].

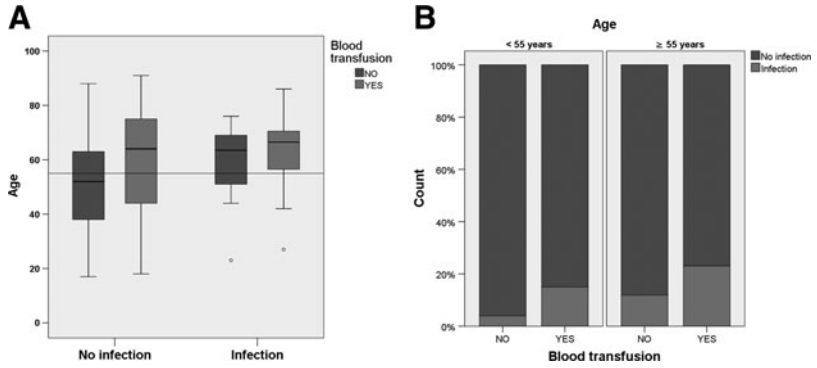

FIG. 1. Effect pre-operative blood transfusion and age on surgical site infection rate. (**A**) Pre-operative blood transfusion was associated with a higher infection rate independently of age. (**B**) Older patients (≥ 55 years) were more likely to have a surgical site infection.

Other studies on this issue investigated outcomes after general surgery. An increase in post-operative infection rates after blood transfusion has been described for patients with colorectal cancer undergoing surgery [15]. By contrast, a large study on risk factors for SSI after general surgery could not find an increase in infections in patients with pre-operative anemia or transfusion [12].

Spinal incisions may be different from those in general surgery. The incision cavities after spinal fusion surgery frequently are large and deep, with extensive surfaces. Surgical site infection, therefore, is more common after spinal fusion surgery, the rate ranging from 4.5%–17% [4,6,8,21,22] vs. 0.3% to 6.8% in general surgery [12,23,24]. This might be an explanation for certain risk factors gaining statistical relevance only in patients having spine surgery.

There are three possible mechanisms that could explain the association of pre-operative allogeneic blood transfusion and SSI. The first is that patients who required blood transfusions had previous loss of blood and therefore had lower oxygen and nutrition transporters to support appropriate healing. As in other studies on this issue [12,14], the difference between patients with and without incisional infection with regard to pre-operative hemoglobin concentration and hematocrit was marginal. Thus, the hypothesis of an undersupply of oxygen and nutrients as a result of blood loss is unlikely, at least in institutions with appropriate peri-operative transfusion management.

In a population of trauma patients or those with metastatic disease, the second possible mechanism is an immunosuppressive effect by the trauma or malignant disease. This has been described especially for the multiply injured patient [25] and patients with spinal cord injuries [26]. It is a limitation of this study that because of the retrospective design, we were not able to evaluate the severity and modalities of the injuries. However, a three- to four-fold higher risk of SSI after pre-operative allogeneic blood transfusions has been reported for non-trauma patients as well [14,15]. Metastatic disease fractures as the cause of spinal instability were not linked to higher SSI rates, either in our study or in the literature [27,28]. It might be, however, that the present study underestimates the influence of malignant disease on SSI, as 80% of the cases analyzed were trauma patients rather than those with malignant disease.

The third possible mechanism of the association of pre-operative blood transfusion and SSI is an immunosuppressive effect as a reaction to the allogeneic transfusion itself. This effect has been discussed to a great extent in the recent literature [15–17]. As red blood cells lyse during storage of blood units, free heme is released as a result of hemoglobin oxidation. As shown in a mouse sepsis model, this free circulating heme increases inflammation and cell death, thereby compromising host tolerance for infection irrespective of the amount of circulating heme [29]. In this context, restrictive transfusion schemes have been able to decrease morbidity and mortality rates in chronically ill patients with euvolemic anemia after acute myocardial infarction [30].

Yet trauma patients or those with metastatic malignant disease undergoing surgery for spinal stabilization are different. Hypovolemic anemia is common in this population, and transfusion management thus has to take care of both an appropriate immediate restoration of blood components and anticipation of future peri-operative and post-operative blood loss. Patients undergoing spinal surgery with blood loss have a six-fold higher risk of SSI if their post-operative hemoglobin concentration is < 8 g/dL [31].

A direct comparison of our results with those of other studies has to be made with caution. Unlike other studies, the present study did not assess intra-operative blood loss, as it was the authors' opinion that the unmeasurable post-operative blood loss is of greater importance to the patient's immune system.

This study assessed only red blood cell transfusions; transfusions of fresh frozen plasma or other plasma components were not recorded. However, the transfusion management in our population of trauma patients followed a fixed algorithm with emphasis on the substitution of factor concentrates to allow a reduction of allogeneic transfusions of red blood cells.

According to the data provided by this study, it is not possible to recommend a particular transfusion algorithm for patients who undergo posterior stabilization of thoracic spine instabilities. Several mechanisms and risk factors may influence the final probability of an SSI. Other aspects, such as blood group compatibility or age and grade of lysis of the blood units, may play an important role and need further evaluation. However, the results of this study point to factors that should be further investigated by basic science trials or in prospective clinical trials with larger subgroup samples.

Conclusion

Subcutaneous fat thickness had no influence on the occurrence of SSI after posterior fusion for the fixation of thoracic spine instabilities, whereas allogeneic red blood cell transfusion within 48 h prior to surgery was an independent risk factor for infection. Specifically, pre-operative blood transfusion tripled the risk of SSI.

Acknowledgment

We thank Prof. Dr. B. Seifert of the Biostatistics Unit, Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland, for his substantial contribution to the statistical analysis of the study data.

Author Disclosure Statement

There were no external sources of funding for this study, and no author has any conflict of interest related to the study.

References

1. Mangram AJ, Horan TC, Pearson ML, et al. Guidelines for Prevention of Surgical Site Infection, 1999. U.S. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control 1999;27:97–132.
2. Poulsen KB, Bremmelgaard A, Sorensen AI, et al. Estimated costs of postoperative wound infections: A case-control study of marginal hospital and social security costs. Epidemiol Infect 1994;113:283–295.
3. Vegas AA, Jodra VM, Garcia ML. Nosocomial infection in surgery wards: A controlled study of increased duration of hospital stays and direct cost of hospitalization. Eur J Epidemiol 1993;9:504–510.
4. Veeravagu A, Patil CG, Lad SP, Boakye M. Risk factors for postoperative spinal wound infections after spinal decompression and fusion surgeries. Spine 2009;34:1869–1872.

5. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopaedic spinal operations. J Bone Joint Surg Am 2008;90:62–69.
6. Roberts FJ, Walsh A, Wing P, et al. The influence of surveillance methods on surgical wound infection rates in a tertiary care spinal surgery service. Spine 1998;23:366–370.
7. Kanayama M, Hashimoto T, Shigenobu K, et al. Effective prevention of surgical site infection using a Centers for Disease Control and Prevention guideline-based antimicrobial prophylaxis in lumbar spine surgery. J Neurosurg Spine 2007;6:327–329.
8. Chaichana KL, Bydon M, Santiago-Dieppa DR, et al. Risk of infection following posterior instrumented lumbar fusion for degenerative spine disease in 817 consecutive cases. J Neurosurg Spine 2014;20:45–52.
9. Wimmer C, Gluch H, Franzreb M, Ogon M. Predisposing factors for infection in spine surgery: A survey of 850 spinal procedures. J Spinal Disord 1998;11:124–128.
10. Mehta AI, Babu R, Sharma R, et al. Thickness of subcutaneous fat as a risk factor for infection in cervical spine fusion surgery. J Bone Joint Surg Am 2013;95:323–328.
11. Tan TW, Farber A, Hamburg NM, et al. Blood transfusion for lower extremity bypass is associated with increased wound infection and graft thrombosis. J Am Coll Surg 2013;216:1005–1014.
12. Junker T, Mujagic E, Hoffmann H, et al. Prevention and control of surgical site infections: Review of the Basel Cohort Study. Swiss Med Wkly 2012;142:w13616.
13. Walz JM, Paterson CA, Seligowski JM, Heard SO. Surgical site infection following bowel surgery: A retrospective analysis of 1,446 patients. Arch Surg 2006;141:1014–1018.
14. Woods BI, Rosario BL, Chen A, et al. The association between perioperative allogeneic transfusion volume and postoperative infection in patients following lumbar spine surgery. J Bone Joint Surg Am 2013;95:2105–2110.
15. Acheson AG, Brookes MJ, Spahn DR. Effects of allogeneic red blood cell transfusions on clinical outcomes in patients undergoing colorectal cancer surgery: A systematic review and meta-analysis. Ann Surg 2012;256:235–244.
16. Taylor RW, Manganaro L, O'Brien J, et al. Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient. Crit Care Med 2002;30:2249–2254.
17. Raghavan M, Marik PE. Anemia, allogenic blood transfusion, and immunomodulation in the critically ill. Chest 2005; 127:295–307.
18. Theusinger OM, Stein P, Spahn DR. Applying ''patient blood management'' in the trauma center. Curr Opin Anaesthesiol 2014;27:225–232.
19. Fujii T, Tsutsumi S, Matsumoto A, et al. Thickness of subcutaneous fat as a strong risk factor for wound infections in elective colorectal surgery: Impact of prediction using preoperative CT. Dig Surg 2010;27:331–335.
20. Tsukada K, Miyazaki T, Kato H, et al. Body fat accumulation and postoperative complications after abdominal surgery. Am Surg 2004;70:347–351.
21. Godil SS, Parker SL, O'Neill KR, et al. Comparative effectiveness and cost-benefit analysis of local application of vancomycin powder in posterior spinal fusion for spine trauma: Clinical article. J Neurosurg Spine 2013;19:331–335.
22. O'Neill KR, Smith JG, Abtahi AM, et al. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. Spine J 2011;11:641–646.
23. Owens PL, Barrett ML, Raetzman S, et al. Surgical site infections following ambulatory surgery procedures. JAMA 2014;311:709–716.
24. Fraccalvieri D, Kreisler Moreno E, Flor Lorente B, et al. Predictors of wound infection in elective colorectal surgery: Multicenter observational case-control study. Cir Esp 2014;92:478–484.
25. Stahel PF, Smith WR, Moore EE. Role of biological modifiers regulating the immune response after trauma. Injury 2007;38:1409–1422.
26. Leicht CA, Goosey-Tolfrey VL, Bishop NC. Spinal cord injury: Known and possible influences on the immune response to exercise. Exer Immunol Rev 2013;19:144–163.
27. Demura S, Kawahara N, Murakami H, et al. Surgical site infection in spinal metastasis: Risk factors and countermeasures. Spine 2009;34:635–639.
28. Omeis IA, Dhir M, Sciubba DM, et al. Postoperative surgical site infections in patients undergoing spinal tumor surgery: Incidence and risk factors. Spine 2011;36:1410–1419.
29. Larsen R, Gozzelino R, Jeney V, et al. A central role for free heme in the pathogenesis of severe sepsis. Sci Transl Med 2010;2:51ra71.
30. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care: Transfusion requirements in critical care investigations. Canadian Critical Care Trials Group. N Engl J Med 1999;340:409–417.
31. Pull ter Gunne AF, Skolasky RL, Ross H, et al. Influence of perioperative resuscitation status on postoperative spine surgery complications. Spine J 2010;10:129–135.

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